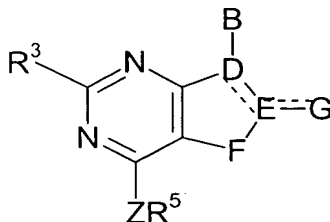


**In the Claims:**

Please cancel claim 22 without prejudice.

Please amend claims 18, 20, 21, 23, and 24 as follows:

18. (Twice amended) A compound of the formula



I

wherein the dashed lines represent optional double bonds;

B is  $-\text{NR}^1\text{R}^2$ ,  $-\text{CR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{C}(=\text{CR}^2\text{R}^{11})\text{R}^1$ ,  $-\text{NHCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{OCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{SCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{CR}^2\text{R}^{10}\text{NHR}^1$ ,  $-\text{CR}^2\text{R}^{10}\text{OR}^1$ ,  $-\text{CR}^2\text{R}^{10}\text{SR}^1$  or  $-\text{COR}^2$ ;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E, or D is CH and is single bonded to E;

F is [oxygen, sulfur,]  $\text{CHR}^4$  or  $\text{NR}^4$  when it is single bonded to E; provided that at least one of D and E is nitrogen or F is  $\text{NR}^4$ , and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is  $\text{NR}^4$ ;

G, when single bonded to E, is hydrogen,  $\text{C}_1\text{-C}_4$  alkyl,  $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $\text{NH}_2$ ,  $-\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$  or  $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$ , wherein each of the  $\text{C}_1\text{-C}_4$  alkyl groups of G may optionally be substituted with one hydroxy,  $-\text{O}(\text{C}_1\text{-C}_2 \text{ alkyl})$  or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

$\text{R}^1$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl optionally substituted with one or two substituents  $\text{R}^8$  independently selected from hydroxy, fluoro, chloro, bromo, iodo,  $\text{C}_1\text{-C}_4$  alkoxy,  $\text{CF}_3$ ,  $-\text{C}(=\text{O})\text{O}(\text{C}_1\text{-C}_4)\text{alkyl}$ ,  $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ ,  $-\text{NHCO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CON}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ ,  $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{SO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$  and  $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ , wherein a carbon-carbon single bond of each of the  $\text{C}_1\text{-C}_4$  alkyl groups in the foregoing  $\text{R}^1$  groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the  $\text{C}_1\text{-C}_4$

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alkyl groups in the foregoing  $R^1$  groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond;  $R^2$  is  $C_1$ - $C_{12}$  alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or  $R^2$  is aryl or  $(C_1$ - $C_4$  alkylene)aryl, wherein said aryl and the aryl moiety of said  $(C_1$ - $C_4$  alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or  $R^2$  is  $C_3$ - $C_8$  cycloalkyl or  $(C_1$ - $C_6$  alkylene)( $C_3$ - $C_8$  cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said  $(C_1$ - $C_6$  alkylene)( $C_3$ - $C_8$  cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^2$  wherein  $Z^2$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, benzyl and  $C_1$ - $C_4$  alkanoyl, and wherein each of the foregoing  $R^2$  groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and  $C_1$ - $C_4$  alkyl, or with one substituent selected from bromo, iodo,  $C_1$ - $C_6$  alkoxy,  $-OC(=O)(C_1$ - $C_6$  alkyl),  $-OC(=O)N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $-S(C_1$ - $C_6$  alkyl), amino,  $-NH(C_1$ - $C_2$  alkyl),  $-N(C_1$ - $C_2$  alkyl)( $C_1$ - $C_4$  alkyl),  $-N(C_1$ - $C_4$  alkyl)- $CO$ -( $C_1$ - $C_4$  alkyl),  $-NHCO(C_1$ - $C_4$  alkyl),  $-COOH$ ,  $-COO(C_1$ - $C_4$  alkyl),  $-CONH(C_1$ - $C_4$  alkyl),  $-CON(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $-SH$ ,  $-CN$ ,  $-NO_2$ ,  $-SO(C_1$ - $C_4$  alkyl),  $-SO_2(C_1$ - $C_4$  alkyl),  $-SO_2NH(C_1$ - $C_4$  alkyl) and  $-SO_2N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl);

$-NR^1R^2$  or  $-CR^1R^2R^{10}$  may form a saturated 3 to 8 membered ring that, in the case of  $-CR^1R^2R^{10}$ , is carbocyclic, and that, in the case of  $-NR^1R^2$ , contains a single heteroatom, nitrogen, which ring may optionally contain from one to three double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^3$  wherein  $Z^3$  is hydrogen,  $C_1$ - $C_4$  alkyl, benzyl or  $C_1$ - $C_4$  alkanoyl;

$R^3$  is hydrogen,  $C_1$ - $C_4$  alkyl,  $-O(C_1$ - $C_4$  alkyl), chloro, fluoro, bromo, iodo,  $-CN$ ,  $-S(C_1$ - $C_4$  alkyl) or  $-SO_2(C_1$ - $C_4$  alkyl) wherein each of the  $(C_1$ - $C_4$  alkyl) moieties in the foregoing  $R^3$  groups may optionally be substituted with one substituent  $R^9$  selected from hydroxy, fluoro and  $(C_1$ - $C_2$  alkoxy);

each  $R^4$  is, independently, hydrogen,  $(C_1$ - $C_6$  alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro,  $-O(C_1$ - $C_4$  alkyl),  $-N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl), -

Et  
Sub  
Fi  
S(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)H or -C(=O)O(C<sub>1</sub>-C<sub>4</sub>alkyl), wherein one or two of the carbon-carbon single bonds in each of the (C<sub>1</sub>-C<sub>6</sub> alkyl) and (C<sub>1</sub>-C<sub>4</sub> alkyl) moieties in the foregoing R<sup>4</sup> groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of these moieties may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C<sub>1</sub>-C<sub>3</sub> alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH<sub>3</sub>, fluoro, chloro, C<sub>1</sub>-C<sub>3</sub> alkylthio, -CN, -COOH, -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl) and -NO<sub>2</sub>;

R<sup>5</sup> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ<sup>4</sup> wherein Z<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl or benzyl; and wherein each of the foregoing R<sup>5</sup> groups is substituted with from one to four substituents R<sup>12</sup> wherein one to three of said substituents may be selected, independently, from chloro, C<sub>1</sub>-C<sub>6</sub> alkyl and -O(C<sub>1</sub>-C<sub>6</sub> alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF<sub>3</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>6</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl], and wherein a carbon-carbon single bond of each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond]; and furthermore wherein when R<sup>5</sup> is phenyl or pyridyl substituted with two or three substituents, said substituents can further be selected from (C<sub>1</sub>-C<sub>4</sub> alkyl)O(C<sub>1</sub>-C<sub>4</sub> alkyl), OCF<sub>3</sub>, and fluoro, and one carbon-carbon single bond of each (C<sub>1</sub>-C<sub>4</sub>) alkyl group of said substituents having between two and four carbon atoms may be optionally replaced with a carbon-carbon double or triple bond; or R<sup>5</sup> is pyrimidyl substituted by two or three substituents independently selected from C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), CF<sub>3</sub>, OCF<sub>3</sub>, -CHO, (C<sub>1</sub>-C<sub>4</sub> alkyl)-OH, CN, Cl, F, Br, I and NO<sub>2</sub>, wherein a carbon-carbon single bond of said (C<sub>1</sub>-C<sub>4</sub>) alkyl groups having between two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond;

~~R<sup>7</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, halo, cyano, hydroxy, -O(C<sub>1</sub>-C<sub>4</sub> alkyl) -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -OCF<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>2</sub>OH, -CH<sub>2</sub>O(C<sub>1</sub>-C<sub>4</sub> alkyl);~~

~~R<sup>10</sup> is hydrogen, hydroxy, methoxy or fluoro;~~

~~R<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and~~

~~with the proviso that: (a) when R<sup>4</sup> is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;~~

~~Z is NH, oxygen, sulfur, -N(C<sub>1</sub>-C<sub>4</sub> alkyl), -NC(=O)(C<sub>1</sub>-C<sub>2</sub> alkyl), NC(=O)O(C<sub>1</sub>-C<sub>2</sub> alkyl) or CR<sup>13</sup>R<sup>14</sup> wherein R<sup>13</sup> and R<sup>14</sup> are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R<sup>13</sup> and R<sup>14</sup> can be cyano;~~

~~or a pharmaceutically acceptable salt of such compound.~~

~~20. (Twice amended) A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease, ] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate [antidiarrhetic] antidiuretic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, psychosocial dwarfism, and hypoglycemia in a mammal, comprising an amount of a compound according to claim 18 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.~~

~~21. (Twice amended) A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an~~

*E2*  
inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate [antidiarrhetic] antidiuretic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim 18, that is effective in treating such disorder.

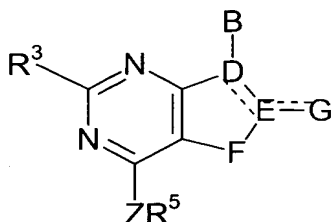
*E3*  
23. (Amended) A pharmaceutical composition for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF; or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, ulcers, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate [antidiarrhetic] antidiuretic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral

sclerosis, psychosocial dwarfism, and hypoglycemia in a mammal, comprising an amount of a compound according to claim [22] 25 that is effective in the treatment of such disorder, and a pharmaceutically acceptable carrier.

24. (Amended) A method for the treatment of (a) a disorder the treatment of which can be effected or facilitated by antagonizing CRF, or (b) a disorder selected from an inflammatory disease, rheumatoid arthritis, osteoarthritis, pain, asthma, psoriasis, allergies, generalized anxiety disorder, panic, phobias, obsessive-compulsive disorder, post-traumatic stress disorder, hypertension, tachycardia, congestive heart failure, sleep disorders induced by stress, [fibromyalgia,] depression, major depressive disorder, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthemia, bipolar disorder, cyclothymia, fatigue syndrome, stress-induced headache, cancer, irritable bowel syndrome, Crohn's disease, spastic colon, human immunodeficiency virus infections, [Alzheimer's disease,] Parkinson's disease, Huntington's disease, anorexia, bulimia nervosa, hemorrhagic stress, stress-induced psychotic episodes, euthyroid sick syndrome, syndrome of inappropriate [antidiarrhetic] antidiuretic hormone, obesity, head traumas, spinal cord trauma, ischemic neuronal damage, excitotoxic neuronal damage, epilepsy, stroke, ulcers, immune suppression, muscular spasms, urinary incontinence, multiinfarct dementia, amyotrophic lateral sclerosis, chemical dependencies and addictions, drug and alcohol withdrawal symptoms, psychosocial dwarfism, and hypoglycemia in a mammal, comprising administering to a subject in need of said treatment an amount of a compound according to claim [22] 25, that is effective in treating such disorder.

Please add the following claim 25:

--25. A compound of the formula



wherein the dashed lines represent optional double bonds;

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Sub F2  
B is  $-\text{NR}^1\text{R}^2$ ,  $-\text{CR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{C}(=\text{CR}^2\text{R}^{11})\text{R}^1$ ,  $-\text{NHCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{OCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{SCR}^1\text{R}^2\text{R}^{10}$ ,  $-\text{CR}^2\text{R}^{10}\text{NHR}^1$ ,  $-\text{CR}^2\text{R}^{10}\text{OR}^1$ ,  $-\text{CR}^2\text{R}^{10}\text{SR}^1$  or  $-\text{COR}^2$ ;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E, or D is CH and is single bonded to E;

F is oxygen, sulfur,  $\text{CHR}^4$  or  $\text{NR}^4$  when it is single bonded to E; provided that at least one of D and E is nitrogen or F is  $\text{NR}^4$ , and provided that only one of D and E is nitrogen, and D and E are not nitrogen when F is  $\text{NR}^4$ ;

G, when single bonded to E, is hydrogen,  $\text{C}_1\text{-C}_4$  alkyl,  $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $\text{NH}_2$ ,  $-\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$  or  $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$ , wherein each of the  $\text{C}_1\text{-C}_4$  alkyl groups of G may optionally be substituted with one hydroxy,  $-\text{O}(\text{C}_1\text{-C}_2 \text{ alkyl})$  or fluoro group; and G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

$\text{R}^1$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl optionally substituted with one or two substituents  $\text{R}^8$  independently selected from hydroxy, fluoro, chloro, bromo, iodo,  $\text{C}_1\text{-C}_4$  alkoxy,  $\text{CF}_3$ ,  $-\text{C}(=\text{O})\text{O}(\text{C}_1\text{-C}_4)\text{alkyl}$ ,  $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ ,  $-\text{NHCO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CON}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ ,  $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{SO}(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$ ,  $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$  and  $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$ , wherein a carbon-carbon single bond of each of the  $\text{C}_1\text{-C}_4$  alkyl groups in the foregoing  $\text{R}^1$  groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the  $\text{C}_1\text{-C}_4$  alkyl groups in the foregoing  $\text{R}^1$  groups having four carbons may optionally be replaced with a carbon-carbon double or triple bond;  $\text{R}^2$  is  $\text{C}_1\text{-C}_{12}$  alkyl wherein one carbon-carbon single bond of any said alkyl having at least two carbons, one or two carbon-carbon single bonds of any said alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond, or  $\text{R}^2$  is aryl or  $(\text{C}_1\text{-C}_4 \text{ alkylene})\text{aryl}$ , wherein said aryl and the aryl moiety of said  $(\text{C}_1\text{-C}_4 \text{ alkylene})\text{aryl}$  is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or  $\text{R}^2$  is  $\text{C}_3\text{-C}_8$  cycloalkyl or  $(\text{C}_1\text{-C}_6 \text{ alkylene})(\text{C}_3\text{-C}_8 \text{ cycloalkyl})$ , wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said  $(\text{C}_1\text{-C}_6 \text{ alkylene})(\text{C}_3\text{-C}_8$

g4  
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cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^2$  wherein  $Z^2$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, benzyl and  $C_1$ - $C_4$  alkanoyl, and wherein each of the foregoing  $R^2$  groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and  $C_1$ - $C_4$  alkyl, or with one substituent selected from bromo, iodo,  $C_1$ - $C_6$  alkoxy,  $-OC(=O)(C_1-C_6 \text{ alkyl})$ ,  $-OC(=O)N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ,  $-S(C_1-C_6 \text{ alkyl})$ , amino,  $-NH(C_1-C_2 \text{ alkyl})$ ,  $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})-CO-(C_1-C_4 \text{ alkyl})$ ,  $-NHCO(C_1-C_4 \text{ alkyl})$ ,  $-COOH$ ,  $-COO(C_1-C_4 \text{ alkyl})$ ,  $-CONH(C_1-C_4 \text{ alkyl})$ ,  $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ,  $-SH$ ,  $-CN$ ,  $-NO_2$ ,  $-SO(C_1-C_4 \text{ alkyl})$ ,  $-SO_2(C_1-C_4 \text{ alkyl})$ ,  $-SO_2NH(C_1-C_4 \text{ alkyl})$  and  $-SO_2N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ;

$-NR^1R^2$  or  $-CR^1R^2R^{10}$  may form a saturated 3 to 8 membered ring that, in the case of  $-CR^1R^2R^{10}$ , is carbocyclic, and that, in the case of  $-NR^1R^2$ , contains a single heteroatom, nitrogen, which ring may optionally contain from one to three double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered ring may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^3$  wherein  $Z^3$  is hydrogen,  $C_1$ - $C_4$  alkyl, benzyl or  $C_1$ - $C_4$  alkanoyl;

$R^3$  is hydrogen,  $C_1$ - $C_4$  alkyl,  $-O(C_1-C_4 \text{ alkyl})$ , chloro, fluoro, bromo, iodo,  $-CN$ ,  $-S(C_1-C_4 \text{ alkyl})$  or  $-SO_2(C_1-C_4 \text{ alkyl})$  wherein each of the  $(C_1-C_4 \text{ alkyl})$  moieties in the foregoing  $R^3$  groups may optionally be substituted with one substituent  $R^9$  selected from hydroxy, fluoro and  $(C_1-C_2 \text{ alkoxy})$ ;

each  $R^4$  is, independently, hydrogen,  $(C_1-C_6 \text{ alkyl})$ , fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro,  $-O(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ,  $-S(C_1-C_4 \text{ alkyl})$ ,  $-SO(C_1-C_4 \text{ alkyl})$ ,  $-SO_2(C_1-C_4 \text{ alkyl})$ ,  $-CO(C_1-C_4 \text{ alkyl})$ ,  $-C(=O)H$  or  $-C(=O)O(C_1-C_4 \text{ alkyl})$ , wherein one or two of the carbon-carbon single bonds in each of the  $(C_1-C_6 \text{ alkyl})$  and  $(C_1-C_4 \text{ alkyl})$  moieties in the foregoing  $R^4$  groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of these moieties may optionally be substituted with one or two substituents independently selected from hydroxy, amino,  $C_1$ - $C_3$  alkoxy, dimethylamino, methylamino, ethylamino,  $-NHC(=O)CH_3$ , fluoro, chloro,  $C_1$ - $C_3$  alkylthio,  $-CN$ ,  $-COOH$ ,  $-C(=O)O(C_1-C_4 \text{ alkyl})$ ,  $-C(=O)(C_1-C_4 \text{ alkyl})$  and  $-NO_2$ ;

$R^5$  is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or  $C_3$ - $C_8$  cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an

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oxygen or sulfur atom or by  $NZ^4$  wherein  $Z^4$  is hydrogen,  $C_1-C_4$  alkyl or benzyl; and wherein each of the foregoing  $R^5$  groups is substituted with from one to four substituents  $R^{12}$  wherein one to three of said substituents may be selected, independently, from chloro,  $C_1-C_6$  alkyl and  $-O(C_1-C_6 \text{ alkyl})$  and one of said substituents may be selected from bromo, iodo, formyl,  $-CN$ ,  $-CF_3$ ,  $-NO_2$ ,  $-NH_2$ ,  $-NH(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_2 \text{ alkyl})(C_1-C_6 \text{ alkyl})$ ,  $-C(=O)O(C_1-C_4 \text{ alkyl})$ ,  $-C(=O)(C_1-C_4 \text{ alkyl})$ ,  $-COOH$ ,  $-SO_2NH(C_1-C_4 \text{ alkyl})$ ,  $-SO_2N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$ ,  $-SO_2NH_2$ ,  $-NHSO_2(C_1-C_4 \text{ alkyl})$ ,  $-S(C_1-C_6 \text{ alkyl})$  and  $-SO_2(C_1-C_6 \text{ alkyl})$ , and wherein each of the  $C_1-C_4$  alkyl and  $C_1-C_6$  alkyl moieties in the foregoing  $R^5$  groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

$R^7$  is hydrogen,  $C_1-C_4$  alkyl, halo, cyano, hydroxy,  $-O(C_1-C_4 \text{ alkyl})$ ,  $-C(=O)(C_1-C_4 \text{ alkyl})$ ,  $-C(=O)O(C_1-C_4 \text{ alkyl})$ ,  $-OCF_3$ ,  $-CF_3$ ,  $-CH_2OH$ ,  $-CH_2O(C_1-C_4 \text{ alkyl})$ ;

$R^{10}$  is hydrogen, hydroxy, methoxy or fluoro;

$R^{11}$  is hydrogen or  $C_1-C_4$  alkyl; and

with the proviso that: (a) when  $R^4$  is attached to nitrogen, it is not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

Z is NH, oxygen, sulfur,  $-N(C_1-C_4 \text{ alkyl})$ ,  $-NC(=O)(C_1-C_2 \text{ alkyl})$ ,  $NC(=O)O(C_1-C_2 \text{ alkyl})$  or  $CR^{13}R^{14}$  wherein  $R^{13}$  and  $R^{14}$  are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of  $R^{13}$  and  $R^{14}$  can be cyano;

or a pharmaceutically acceptable salt of such compound.---